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ABSTRACTS

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AMERICAN REVIEW OF TUBERCULOSIS ABSTRACTS

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Incidence of Tuberculous Infection.—In the early part of the present century the "universality of tuberculous infection" was generally accepted chiefly as a result of the classical postmortem studies of Naegeli (1900) and others. With the introduction of the cutaneous tuberculin test (von Pirquet) further evidence was obtained to support the impression gained from these anatomical studies. In a number of surveys in European cities the great majority of children by the age of fifteen years or less were found sensitive to tuberculin. Now, however, most authors agree that whereas the vast majority of primary infections formerly occurred in childhood, this is no longer true, at least not in the United States. The low incidence of positive reactions in many recent tuberculin surveys and especially in communities which formerly gave a high incidence appear to make the earlier concept untenable. It has been conceived that the sharp decline in mortality and morbidity from the disease, which has characterized the modern era, has reduced the number of infective cases as greatly to lower the rate of exposure, even to a point where many individuals may never be exposed. But it must be borne in mind that these tuberculin surveys tested mostly children and young people and have not been representative of the community as a whole. Furthermore, it has been found experimentally that hypersensitivity wanes following a well resisted infection unless it is reanimated by subsequent fresh infections. Hence the marked reduction in the number of open cases of tuberculosis in the present day population may reduce the exposure rate sufficiently to allow many infected individuals to lose their hypersensitivity by escaping these reanimating reinfections. In support of this it has recently been found that an appreciable number of tuberculin-negative individuals show evidence of healed tuberculous lesions by X-ray and, moreover, the percentage of individuals who have been observed to lose their tuberculin sensitivity is much higher now than formerly. In view of these limitations of the tuberculin test as an indicator of the incidence of infection it was decided to resort to the original method of post-mortem anatomical search in the attempt to establish this incidence. This method of investigation was employed on a representative sample of the autopsies in two large hospitals in the City of Baltimore during the period 1938 to 1940. In all it comprised 536 cases of the autopsied deaths and includes all ages. All cases in which tuberculosis was the major cause of death were excluded from the series. The complete omission of fatal cases of tuberculosis causes no significant error in the observed incidence of infected individuals in any age group in which the true incidence of infection itself is high in relation to the mortality rate. The technique of the examination was essentially the same as first employed by Opie in a similar survey in St. Louis and reported in 1916. Either before or after fixation, the entire lungs, together with the tracheal and bronchial lymph nodes, and as many of the cervical nodes as could be obtained, were X-rayed and later examined with the X-ray film as a guide. This method quickly discloses most of the lesions. When

no suspicious lesions were disclosed by the film, serial thin slicing of material was done after hardening in Keiserling's solution. All lesions of uncertain tuberculous nature were sectioned for microscopical examination. The findings from this investigation indicate that 70 per cent of the individuals in Baltimore have acquired a tuberculous infection by the age 20 and that universal infection is approximated only in the age group above 50 years. Taking into consideration the age distribution of the adult population the data indicate that about 90 per cent of the adults in Baltimore have been infected. While these results suggest a moderate fall in the incidence of infection in adults since the study of Opie in St. Louis, the statistical comparison does not yield a conclusive answer. For instance, Opie's findings indicated 80 per cent infection at twenty years and 100 per cent infection at about 35 years, whereas in the present study the percentage is approximately 65 and 85 respectively. But the number of individuals examined by Opie in each age group from 2 to 30 years is so small as to make the observed percentages of very low reliability. Similar anatomical investigations carried out in European cities since the beginning of the century show considerable local differences in the incidence of infection. The more recent European surveys have not shown any great change in spite of a marked decline in tuberculosis mortality. Similar anatomical surveys should be conducted in various parts of the United States before any conclusion is reached regarding the prevalence of tuberculous infection in this country today. A comparison between the available tuberculin surveys and the anatomical findings suggests that the great decrease in the rate of exposures of the population in recent times may have resulted in a greater decrease in the number of infected persons who maintain their hypersensitivity to tuberculin than in the proportion of infected individuals.—*The Present Incidence of Tuberculous Infection, W. H. Carnes, Bull. Johns Hopkins Hosp., February, 1942, 70: 101.*—(*J. S. W.*)

Tuberculosis Control by State Agencies.—A nation-wide survey of the participation of official State agencies in the various tuberculosis programs is presented and discussed. It is shown that the tuberculosis programs carried on at the State level differ widely in policy and content. The presence or absence of State services of different categories are tabulated. In contradistinction to the control of general communicable diseases state responsibility in tuberculosis control is dispersed. In only 13 States single-agency programs are found. In about half of the States two agencies participate in tuberculosis activities and in the remaining States the programs are administered by three or more governmental units. The activities of these agencies are frequently unrelated. This lack of coördination becomes particularly noticeable when hospital program and field activities are carried out by separate agencies. Even within the hospital program there is divided control in certain States. State programs may include any one or any combination of the following functions: regulatory authority, promotional and educational activity, advisory and supervisory assistance to local units, financial subsidy of local tuberculosis work or provision of direct state service. There is extreme variation in the type of direct service provided. The approximate expenditures on services designated for tuberculosis total nearly 25 million dollars and average somewhat less than $400.00 per tuberculosis death for the nation as a whole. The range, however, is very wide. In 16 States these expenditures are limited to less than $200.00 per tuberculosis death and in 12 States they exceed $1000. It is shown that a State's purchasing power has a direct bearing on the amount expended for tuberculosis control. The content of the program is also influenced by the economic status. Poorer States allot a larger proportion of their total expenditures to field service, than do wealthy ones; probably because they find it difficult to finance hospitalization with any degree of adequacy, this being the most expensive item in the complete tuberculosis program.—*Distribution*

of Health Services in the Structure of State Government. Chapter III. Tuberculosis Control by State Agencies, J. W. Mountin & Evelyn Floor, Pub. Health Rep., January 16, 1942, 57: 65.—(*A. B. T.*)

Housing and Tuberculosis.—Data collected in the National Health Survey of 1935–1936 are analyzed to show the relationship of housing conditions to the prevalence of a variety of diseases. Calculation of the secondary attack rate of tuberculosis was made in families with one person or less per room, with 1 to 1.5 persons per room and with more than 1.5 persons per room. An attempt was made to eliminate the factor of income by adjustment to a standard income distribution. The excess in the secondary attack rate in the crowded households was less than 20 per cent. Comparison of the rate in families receiving public assistance showed about a 60 per cent excess in the crowded households. In all households, the excess in secondary attack rate in the crowded families was especially marked in children under fifteen years of age. In this age group the incidence was 80 per cent greater in crowded households.—*New Light on the Relation of Housing to Health, R. H. Britten, Am. J. Pub. Health, February, 1942, 32: 193.*—(*H. L. I.*)

Willingness to Be Examined for Tuberculosis.—In the course of a special case-finding program in Detroit 187,543 individuals of known age and color were visited by public health nurses who urged examination. These persons were in the low income group, but the examinations were provided without expense. A satisfactory examination including tuberculin test, with X-ray examination, if the skin test was positive, was completed by 48,179 individuals (25.7 per cent). The best response was obtained in the age group five to fourteen years. For each age group the percentage of response was twice as great among the colored as among the white population. The age of greatest response was not the age of the highest tuberculosis case rates.—*Willingness of Individuals to Be Examined for Tuberculosis, G. E. Harmon, Am. J. Pub. Health, February, 1942, 32: 187.*—(*H. L. I.*)

Case-Finding.—There is as much need for effective tuberculosis control in non-metropolitan areas as in areas of highly concentrated population. The author presents a report on a five year case-finding clinic organized in an Ohio County of 74,000 population, equally divided between urban and rural districts, and draws some conclusions as to effective organization procedures in such areas. In the fifth year 93.8 per cent of the reported cases of tuberculosis were diagnosed in the clinic, as compared with 56 per cent in the first year. During the five years active tuberculosis was discovered in 175 of 1270 new patients examined, pulmonary tuberculosis in 155. This yield (13.7 per cent) is too high, although the rate has been steadily decreasing, and indicates that physicians should be encouraged to refer a larger number of patients to the clinic. During the five years the percentage discovered with far advanced disease has decreased from 77 to 43 and the percentage with incipient disease has risen from 13 to 34. In a comparison of tuberculosis among contacts and among suspects, 58 per cent of the discovered tuberculosis in the former group was in the incipient stage, as compared with 29 per cent in the group of suspects. As a measure of aroused public interest, each year the sale of Christmas seals has increased, and a public 0.5 mill tax levy has been in operation since 1938 to raise necessary funds for treatment. The following lessons may be derived from the Richland County experience: There is no reason to defer the setting up of a case-finding program because there is no sanatorium in the district. The author believes that the tuberculosis hospital as a county project is not economically sound except in metropolitan areas. The program should be based on the county unit and should be operated as a permanent part of the county health department, and, if any exist, of the city health departments. The program should be run in coöperation with private physicians on a referral basis. Thus there is a

logical and reasonable division of labor between the private physician and the clinic, with each supplementing and complementing the other. The clinic physician must be an adequately trained chest specialist and tuberculosis epidemiologist. With such a program as outlined, it is possible to keep the cost per case found within reasonable limits and still approach an adequate coverage of the area.—*Tuberculosis Case-Finding, T. L. Bliss, J. A. M. A., December 6, 1941, 117: 1944.*—(*G. L. L.*)

Fluorographic Screening for Tuberculosis.—Efforts to prevent the occurrence of tuberculosis rest largely on limiting the spread of the tubercle bacilli. Since bovine tuberculosis has been so well controlled in this country the one remaining source of the tubercle bacilli is patients with open tuberculosis. Therefore it is important to detect all cases of tuberculosis in a community. A familiar method for doing this is the use of tuberculin skin tests and roentgenological examination of reactors. Because of the expense of the roentgen-ray examination less expensive methods have been sought. For the past two years a fluorographic method has been used in Detroit. This method employs a camera capable of making a photograph of the fluorescent image on a 4 x 5 inch film. This size film is used since it is large enough to be readily interpreted without enlargement and yet small enough to be relatively inexpensive. At least a 200 milliampere roentgen tube must be used and better results are obtained if a rotating anode tube allowing the use of 400 milliamperes is used. An error of 2.6 per cent in failure to detect certain very small lesions by this method was found when a large number of patients were examined with the regular size film and the small fluorographic film. In a series of 6,104 small films it was found necessary to call back only 51 persons for recheck on regular size film. By this method 15,220 individuals were examined and of this number 163 were found to have active tuberculosis. Of these 27 had primary infections, 45 minimal tuberculosis, 42 moderately advanced disease, 32 far advanced disease, 3 miliary tuberculosis and 14 had pleural effusions. The fluorographic method is an accurate way to make roentgen-ray examinations of the chest and it is believed that wider use of this method will aid in the control of tuberculosis through better case-finding.—*Screening for Tuberculosis in a Civilian Population by Fluorography, B. H. Douglas & C. C. Birkelo, Ann. Int. Med., November, 1941, 15: 853.*—(*A. A. E.*)

Tuberculosis in Contacts.—The prevalence of infection and disease has been compared among household associates of Negro index cases with that found among the associates of white index cases in a study in Williamson County, Tennessee. Among families in which the index case had positive sputum (or died of tuberculosis) the percentage of reactors to tuberculin was considerably higher than among families in which the index case was sputum-negative. There was close agreement in the prevalence of infection in the white and Negro groups. The prevalence of manifest tuberculosis at the time of investigation was approximately the same among white and Negro household associates of the open, or presumably open, index cases. Cases found among the Negro contacts were, however, more often in an advanced stage and were more often rapidly fatal. Manifest tuberculosis was infrequent among the associates of sputum-negative index cases. The frequency of latent apical tuberculosis was lower among Negroes than whites under similar conditions of exposure. The authors point out that the total prevalence of pulmonary tuberculosis at any given time may be lower in colored families because manifest cases are eliminated more rapidly from the colored population.—*Tuberculosis Studies in Tennessee. Prevalence of Tuberculosis Infection and Disease in White and Colored Families as Revealed at the Time of Investigation, R. R. Puffer, R. S. Gass, W. J. Murphy & W. C. Williams, Am. J. Hyg., 1941, 34: Sec. A., 71.*—(*H. L. I.*)

Tuberculosis in Nurses.—The authors present a study of tuberculous infection in a group of 643 students in the Philadelphia General Hospital training school over a four-year period. On admission, 57 per cent were tuberculin reactors. A rapid rate of infection was noted among the 43 per cent of negative reactors. At the end of four months, 48 per cent of these reacted to tuberculin, at the end of one year 85.9 per cent reacted and at the end of three years 100 per cent reacted. A high incidence of pleurisy with effusion and of pulmonary infiltrations, roentgenologically typical of tuberculosis was observed. The annual attack rate was 4.81 per cent, an incidence slightly higher than that reported in similar large general hospitals. Serious illness from tuberculosis, however, was not proportionately frequent, and no deaths occurred, presumably in part because of prompt treatment. No tuberculous lesions appeared during the first four months of training and only 3 developed during the second four month interval. The attack rate for the entire group rose rapidly thereafter, reaching a maximum in the second year of training; during the third year the attack rate began to decline. Pulmonary tuberculosis or pleurisy with effusion developed in 10.6 per cent of the students at risk. Only slight differences in incidence and in anatomical character and distribution of tuberculosis as determined by roentgenological examination were observed between students who had been tuberculin negative at the onset of observation and students who had been tuberculin positive on admission. Comparison of the subsequent clinical course of students in the two groups showed no difference in the proportions of progressive and retrogressive lesions. The development of a positive tuberculin reaction was associated with a high incidence of nonspecific respiratory, gastrointestinal, febrile and vague toxic illness and with an especially high frequency of abdominal symptoms simulating appendicitis.—*A Study of Tuberculosis among Students of Nursing, H. L. Israel, H. W. Hetherington & J. G. Ord, J. A. M. A., September 6, 1941, 117: 839.*—(*G. L. L.*)

Rehabilitation.—The rehabilitation of tuberculous patients is an important social problem. Many ex-patients are employed in tuberculosis hospitals which is the best solution because of favorable working conditions and medical supervision. There is no evidence that the exposure brings about reactivation of the disease. Several cases are cited where compensation was awarded because physicians stated that reactivation of the disease in their patients was due to their employment. Such decisions are the reasons why several sanatoria now do not employ ex-patients. Some cases of tuberculosis occur among previously healthy hospital employees and the hospitals usually employ them again. More reports are necessary to disseminate the knowledge that exposure does not cause reactivation.—*Arrested Tuberculosis and Hospital Employment, L. Brahdy, J. Indust. Hyg. & Toxicol., March, 1942, 24: 53.*—(*G. C. L.*)

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parents. The treatment of the primary infection in childhood consists of adequate hygiene and diet.—*Prognostic et traitement de la primo-infection, L. Rousseau, Laval méd., February, 1942, 7: 107.*—(*G. C. L.*)

Primary Infection.—At least 75 per cent of tuberculous primary infections in children are caused by family contact. The primary infection is often without symptoms and signs. Allergy develops three to seven weeks after the infection. The most reliable tuberculin test is the Mantoux test. Every tuberculin-positive child should be examined roentgenologically, although the primary focus can often not be seen on the X-ray film. About 50 per cent of children with a primary focus have tubercle bacilli in their gastric juice.—*La primo-infection tuberculeuse de l'enfant, R. Desmeules, Laval méd., February, 1942, 7: 87.*—(*G. C. L.*)

Primary Infection.—Primary tuberculous infection in adults is not as rare as it is believed. The diagnosis of a primary infection has to be made when a person who was tuberculin negative turns positive. The morbidity is higher in the subjects with primary infections than in those who had their primary infection during childhood; however, the disease rarely takes a lethal course.—*La primo-infection tuberculeuse de l'adulte, P. Richard, Laval méd., February, 1942, 7: 93.*—(*G. C. L.*)

Primary Infection.—The tuberculous primary infection takes place in the respiratory tract in about 85 per cent, in the digestive tract in about 15 per cent. Primary infections of skin and genitalia are very rare. Intestinal primary infections are usually due to the bovine bacillus. The bovine type is responsible for 20 to 35 per cent of tuberculous infections in childhood and for 1 to 4 per cent in adults. Only in 0.6 to 2 per cent of the tuberculous adults is the bovine bacillus found. The primary infection depends on the number and virulence of the tubercle bacilli and on the resistance of the organism. If a small number of bacilli reach the lungs of an animal, they are rapidly taken up by macrophages; the bacilli are digested and the cells disappear. If the number of bacilli is large, caseous pneumonia or miliary tuberculosis develops. Infection with a moderate amount of bacilli produces tuberculous foci; their centre caseates, fibrous tissue is formed around them. Either the bacilli die and the foci calcify; or the bacilli remain alive in the caseous centre. When by some disease the allergy of the subject is decreased the foci can turn active; endogenous reinfection may follow which is probably the cause of chronic tuberculosis in the adult. The autopsy findings of three cases are reported: Under the anergy producing effect of infectious diseases from which the patients died, the old primary focus had become reactivated.—*Pathogénie de la primo-infection tuberculeuse, L. Berger, Laval méd., February, 1942, 7: 75.*—(*G. C. L.*)

Pulmonary Cavities.—A study of chest roentgenograms in cavernous tuberculosis was made in an effort to evaluate therapeutic results. The records of all patients with cavities in the Hopemont Sanitarium from July, 1925 to July, 1938 have been studied. Only those patients with at least six months of controlled treatment and in whom a definite cavity could be outlined on the roentgenograms were used. The total number of cases is 750 and in these there were 1,097 cavities. All cases were classified according to the National Tuberculosis Association Classification, but this was modified to apply separately to each lung. Individual cavities were measured in centimeters at the widest diameter on a 6-foot postero-anterior roentgenogram. The roentgen changes in individual cavities were tabulated for patients treated by bed rest, mild activity, phrenic nerve surgery, pneumothorax and thoracoplasty. Cavities were considered closed only when roentgenograms failed to reveal any evidence of open cavities. The same cavity if observed for six or more months under more than one therapeutic procedure has been listed under each procedure. Thus, while the cavities

present in this series total 1,097, the therapeutic results total 1,333. Thirty-five per cent of all cavities were closed, 20 per cent became smaller, 17 per cent remained the same and 28 per cent became larger. Cavities were closed or made smaller more frequently by collapse therapy than by treatment without collapse. Five hundred and twenty-nine cavities were treated by bed-rest, 264 by mild activity, 169 by phrenic nerve surgery, 341 by pneumothorax, and 30 by thoracoplasty. With bed-rest, 13 per cent of the cavities were closed, 25 per cent with mild activity, 24 per cent by phrenic nerve surgery, 76 per cent by pneumothorax, and 93 per cent by thoracoplasty. The greater preponderance of patients with exudative disease and larger total cavitation are included in the group treated by bed-rest, whereas the cases chosen for thoracoplasty were subject to a very conservative selection. In the group that had no collapse therapy, 17 per cent of the cavities were closed. Of those that had collapse treatment of some kind, 61 per cent were closed. There is a higher incidence of closure of cavities among those patients with solitary cavities than among those with multiple cavities. Comparison of the results of various forms of treatment depends in part upon the incidence of exudative pulmonary disease, the average total cavitation present, the average number of months necessary for cavity closure, the average duration of each form of treatment, and the average period of observation after closure of the cavity. In the noncollapse group 34 per cent of the cavities were present in cases showing a predominance of exudative disease, while in the collapse group 32 per cent had predominantly exudative disease. The average total cavitation in the noncollapse group was 11 cm., while in the other group it was 8 cm. Among patients treated without collapse therapy, an average of sixteen months was required for closure of cavities while among those treated by collapse the average period required for closure was eight months. Closure of all pulmonary cavities was obtained in 331 of the 750 cases (44 per cent) in this study. Four hundred and fifty-seven patients had single cavities and of this group closure was effected in 60 per cent. Two hundred and ninety-three had two or more cavities and in these closure was accomplished in 17 per cent. Successful therapeutic results are invariably proportional to the diameter of total pulmonary cavitation, the diameter of the individual cavity and the preponderance of exudative disease. Individual cavities were found to close more readily when they were solitary than when multiple. Collapse therapy required half the time and was three times as effective as noncollapse measures in closing individual cavities.—*A Roentgen Study of Cavities in Pulmonary Tuberculosis; Cavity Changes under Collapse and Noncollapse Measures, R. C. Edson & A. L. Starkey, Ann. Int. Med., October, 1941, 15: 716.*—(*A. A. E.*)

Haematogenous Tuberculosis.—It has long been thought that the primary phase of tuberculosis infection is a purely local affair. However, this is quite untrue. During the first phase of tuberculous infection when there is no sensitivity of the tissues to the proteins of the tubercle bacilli, the bacilli are widely disseminated throughout the body by way of the circulation. This wide dissemination of tubercle bacilli occurs most frequently in the preallergic period that exists in the primary phase of infection. In the guinea pig this preallergic period lasts ten to twelve days after the first implantation of bacilli. In humans the preallergic period probably varies from fourteen days to four months. In the period between the first implantation of the tubercle bacilli and the appearance of specific tissue allergy the bacilli are widely disseminated through the tissues of the animal or human. From the site of the first implantation the bacilli are carried into the lymph vessels and some are filtered out in the neighboring lymph nodes; others pass into the venous circulation and subsequently into the arterial circulation to be implanted in all organs throughout the body. This process continues until the period of tissue allergy has been established. Then, wherever tubercle

bacilli are present in the tissues severe exudative reactions occur. The exudative reaction then may go on to caseation or absorption. In the later phase of the disease after allergy to tuberculoproteins has been established any progressive tuberculosis may be considered reinfection. Reinfection tuberculosis can be defined as a reimplantation of tubercle bacilli in tissues which are allergic to tuberculoproteins. Once tissue allergy has been established general infection along the lymphatics does not occur. Since there is some confusion caused by the use of the terms primary and reinfection tuberculosis, it is proposed that these terms be discarded and that in their stead more specific terms should be used. Thus the preallergic phase describes that period when there is no specific tissue allergy, and the allergic period the later phase after the tissues have been sensitized. Haematogenous dissemination of tubercle bacilli may occur during the period of allergy but does not do so by way of the lymph channels, but by direct invasion of the blood vessels.—*Hematogenous Dissemination of Tubercle Bacilli in Primary and Reinfection Forms of Tuberculosis, G. G. Ornstein, Quart. Bull. Sea View Hosp., July, 1941, 6: 343.*—(*A. A. E.*)

Chronic Miliary Tuberculosis of Lungs.—Types of miliary tuberculosis which are not acute and not always fatal have been described since 1845. A complete description of a type of miliary tuberculosis of subacute character and not always fatal, distinct from, and contrasted with, acute fatal miliary tuberculosis, was published in 1898 by Bard and Paillard. Finally in 1924, Burnand and Sayé described a clinico-radiological picture which they called "granulie froide". This refers to a type of tuberculosis without significant febrile reaction, which is slowly progressive, produces few symptoms and is characterized by multiple tiny nodules of sclerotic character tending to localize in the upper lung fields above the hila. It may terminate with clinical cure plus radiological resolution, or may progress to cavitation and terminal acute dissemination or to cachexia with cardiac disturbances. They attribute the picture to a peribronchial lymphangitic spread comparable to lymphangitic carcinomatosis. Numbers of cases of this character have been published but there is still much difference of opinion as to the propriety of regarding it as a nosological entity. Out of 1,700 cases of tuberculosis, 11 cases presenting the type of picture outlined by Burnand and Sayé could be found. They are described in detail. Five were fatal in from nine months to two years. Four of the the other 6 are known to have lived at least four years. Thus, the outlook of these cases does not differ from that of the general run of cases of tuberculosis. The types of onset were no different from those observed in chronic productive tuberculosis in general. Five began with haemoptysis. Five had cough, chills, loss of weight and appetite. One had dysphonia. They were all characterized by slow progress and constancy of X-ray and physical signs. But close observation showed clinical and, at times, X-ray evidence of brief exacerbations. This is what occurs in all forms of acino-nodular tuberculosis. These 11 patients were between fifteen and forty years of age. Four died of broncho-pneumonia due to intracanalicular spread and the fifth of acute miliary tuberculosis with meningitis. Opportunities to study the anatomical changes in this type of case are rare because of its benign character. There may be a terminal acute alveolitis. The characteristic lesion consists of symmetrically disseminated small proliferative nodules in a fibrous stroma. They are seen in different stages of evolution. They are surrounded by normal alveoli or by localized emphysema depending on their mode of origin. When these lesions become conglomerate, small, dry ulcerations form, not surrounded by inflammatory reaction or atelectasis. In addition there may be any of the other usual tuberculous lesions. The chronic miliary lesions are the result of recurrent bacillaemia with organisms of reduced virulence, occurring on the background of the

tertiary allergy of Ranke. They cannot be clinically distinguished from similar lesions resulting from canalicular spread. The impression of lymphatic spread derives from the fact that, at times, the dissemination is associated with a diffuse pulmonary congestion. In the event of spread by way of the lymphatics, one would expect pleurisy or pericarditis. There is no evidence for the theory of lymphatic spread. The clinical picture is that of any low-grade tuberculosis. The radiological picture of chronic miliary tuberculosis must be distinguished from several similar pictures. Certain types of bronchogenic spread present a similar picture, which, however, is usually asymmetrical and located in the lower part of the lung and exhibits larger nodules with less distinct margins. There is usually more pronounced clinical evidence of disease—more cough, more fever, more physical signs. Silicosis is differentiated by its larger nodules, parahilar localization, history and more pronounced cough and dyspnoea. Pseudomiliary pictures may develop after haemoptysis but are usually in the lower lobes. The history of haemoptysis and the disappearance of the lesions within a relatively short period also distinguishes this from real miliary spread. Mitral disease causes similar pictures, but is readily identified by cardiac enlargement and clinical findings. Miliary carcinomatosis is distinguished by its unilateral localization and by the general clinical picture. Acute miliary tuberculosis is distinguished by the clinical picture. Prognosis and treatment are as for chronic tuberculosis in general.—*Granulias frias, I. M. Hernández & I. Smirnoff, Arch. argent. de tisiol., July-September, 1941, 17: 281.*—(*H. B. S.*)

Prothrombin in Tuberculosis.—To determine the relationship of haemorrhage in tuberculous patients to the prothrombin level in the blood, the author studied a group of 106 patients at the White Haven Sanatorium (10.6 per cent minimal, 20.6 per cent moderately advanced and 69.1 per cent far advanced pulmonary tuberculosis). A significant deficiency of prothrombin was found in 51 patients of the group, 50 of whom had far advanced tuberculosis. In the entire group, 73 per cent with minimal, 60 per cent with moderately advanced and 9.6 per cent with far advanced tuberculosis had a prothrombin concentration within the normal range. Sixty-eight and one-half per cent of those with far advanced tuberculosis had a prothrombin concentration below 59 per cent of normal. There was no constant relation between the prothrombin concentration and the sedimentation rate. It is suggested that the prothrombin concentration should be determined in every case of haemoptysis in pulmonary tuberculosis. In 4 cases of frank haemoptysis with associated prothrombin deficiency, the elevation of the blood prothrombin level on the administration of vitamin K, orally and parenterally, was a likely factor in the control of the haemoptysis.—*Prothrombin Deficiency in Pulmonary Tuberculosis, R. F. Sheely, J.A.M.A., November 8, 1941, 117: 1603.*—(*G. L. L.*)

Tuberculosis and Pregnancy.—The strain that pregnancy puts on a tuberculous patient is discussed and prompt, adequate treatment of the infection is stressed. Close coöperation between the obstetrician and the phthisiologist is urged. Therapeutic abortions may be as hazardous as a normal delivery and are less frequently advocated nowadays when the proper treatment of the tuberculosis is instituted. The pregnant tuberculous patient should be hospitalized and collapse therapy, preferably pneumothorax, started when possible. Pneumothorax should never be discontinued during pregnancy. It may obviate the harmful effect of the rapid descent of the diaphragm following labor. The therapy of 11 cases of pregnancy associated with active pulmonary tuberculosis is briefly described. — *Pulmonary Tuberculosis and Pregnancy, R. H. Baker & A. D. Ward, New England J. Med., February 5, 1942, 226: 224.*—(*J. B.*)

Electrostethography. — The analysis of sounds and vibrations requires visual methods

for detailed study. By listening to chest sounds and seeing their wave forms one becomes aware of finer distinctions and sounds. Recent developments in electronics permit the design of a visual recording apparatus which will accurately record vibrations over wide frequency ranges. An electrostethograph has been devised utilizing a crystal microphone, an electron amplifier and a cathode ray tube recorder. Utilizing phonation on the part of the subject the method permits visual study of chest sounds as well as single photographic exposures. In the normal individual the characteristic wave forms in the upper chest comprise a fundamental frequency and an harmonic. These undergo progressive changes, becoming sine waves at the lower border of the lungs. The lung borders can be accurately outlined. The amplitude of the wave formed is usually greater at the right apex than at the left. Behind the heart on the left there are characteristic remnants of harmonics present which are not seen at the symmetric point on the right side. In pneumothorax an injection of 300 cc. of air reduced the amplitude of the wave at the posterior apex on the injected side 70 per cent as compared with a difference of only 10 per cent before injection. A similar reduction in the amplitude of the wave after refill was found at other points in the chest. Hydrothorax results in a loss of transmission and the reduction of amplitude in the wave may be as much as 90 per cent. Two cases with healed fibrotic apical lesions showed an increase in the amplitude of the waves in the supraclavicular area on the affected side. The phonation method described offers definite refinements in the study of chest sounds and the simplicity of operation and compactness of the instrument make the method a practical one for the study of patients.—*Electrostethography, I. Cathode Ray Visualization of Lung Chest Sounds, F. L. Dunn, W. E. Rahm, Jr., & R. M. Cochran, Ann. Int. Med., March, 1942, 16: 521.*—(*A. A. E.*)

Differential Diagnosis of Pulmonary Infiltrates.—The author has studied the pulmonary lesions of the armed force in Switzerland in all cases where the admission diagnosis of tuberculosis was later shown to be incorrect. He has come across a variety of conditions which have led to consideration of the following differential diagnosis: atypical pneumonia, fleeting infiltrations with eosinophilia, atelectasis, actinomycosis, Wasserman-positive infiltrates, rare forms of bronchitis, such as Castillani's disease, the pulmonary complications of undulant fever, sarcoidosis, lymphogranulomatosis, tumors of the lung. The clinical picture may be that of a haemorrhagic tracheobronchitis in cases of undulant fever and various forms of influenza. These cases are accompanied by marked prostration, a severe course and an abundance of physical signs. The X-ray film shows increased root markings and very fine linear infiltrations. Another variety of clinical appearance is that of enlarged nodes at the hilum. The differentiation from glandular tuberculosis is usually difficult and only long observation will make the diagnosis. The conditions to be considered are residual pneumonic hilar shadows, Boeck's disease and undulant fever. The latter condition is most often diagnosed through serological and sputum examinations. Unresolved pneumonia is extremely difficult to differentiate from tuberculosis. The areas usually involved are the right cardiophrenic region, the retrocardiac space and the perihilar infiltrations. Actinomycosis may be very confusing unless this condition is kept in mind. Lymphogranulomatosis of the lung and carcinoma will occasionally have to be considered. The clinical picture may be that of ordinary bronchitis, but together with massive shadows in the lung the diagnosis of Loeffler's disease may be suspected. Such cases usually are well out of proportion to the radiographic findings and the pronounced eosinophilia will make the diagnosis. The fifth syndrome is that of spontaneous nontuberculous pneumothorax with or without effusion and only prolonged observation will establish the nontuberculous nature.—*Tuberkulose und Armee im Aktivdienst 1939 und folgenden Jahren, III. Zur Differentialdiagnose der Lungenin-*

filtrate, N. Markoff, Schweiz. med. Wchnschr., November 8, 1941, 71: 1420.—(H. M.)

Permanent Collapse Therapy. — In advanced pulmonary tuberculosis with cavitation, frequently the volume of healthy lung is so reduced that it is incapable of occupying the full minimum volume of the thoracic cavity. Satisfactory permanent healing cannot take place under such circumstances, although a few patients may adjust spontaneously to considerable distortion of the thoracic viscera which accompanies the process of extensive scar formation. For a second group the problem has been solved by an adequate pneumothorax which is maintained indefinitely with safety. There is a third group in which thoracoplasty is not applicable. The remainder fall in the fourth group, whose health can be restored with surgical help. In this group temporary measures have failed or present no reasonable chance of being effective. They have an equivalent of two healthy pulmonary lobes, the two on one side or one on each side. Preferably, the disease is stable. The thoracic cage can be refashioned in these cases. A permanent thoracic wall readjustment may in the future come to be looked on as one of the most conservative types of treatment. The author gives the results of a study of 422 patients from various sanatoria who had been treated successfully by thoracoplasty, and who had completed the proper postoperative regimen. A division was made into 107 patients discharged more than five years and 315 discharged less than five years ago. Of the former group, 94.4 per cent were still living, and 3.7 per cent had reactivated. Of the latter group, 97.8 per cent were still alive, and 5.7 per cent had reactivated. These results are considerably more satisfactory than the survival rate in reports of other series, including all types of patients leaving the sanatorium with consent, and even higher than the survival rate of patients entering with minimal disease. The permanent collapse provided by thoracic wall readjustment appears to give the advanced patient better protection against reactivation and a better chance for a lasting result under conditions of moderate activity. The great majority of post-thoracoplasty patients are able to work. Of 293 patients in this group who replied to a questionnaire, 83 per cent had been working for an average of twenty three months, and 91 per cent considered themselves well. Among the benefits of the modern thoracoplasty are the possibility of adjusting the thoracic volume to equal the volume of the remaining healthy lung, the fact that the procedure may be highly selective for disease and is applicable bilaterally, and the risk of tuberculous or mixed empyema or spontaneous pneumothorax is greatly lessened. Refinements of the operation that have added to its effectiveness include lung palpation at operation, specific mobilization and the liberation of anchoring structures over areas of disease, preservation of periosteal elements and subtotal scapulectomy to minimize deformity in partial thoracoplasty.—*Permanent Collapse Therapy in Pulmonary Tuberculosis, R. H. Overholt, J.A.M.A., November 15, 1941, 117: 1681.—(G. L. L.)*

Thoracogenic Scoliosis.—A large number of patients who have had extrapleural thoracoplasty for the treatment of pulmonary tuberculosis develop spinal curvatures as a result of the operation. In most cases scoliosis is of a moderate degreee, although even in such patients the disfigurement may be of great concern. A roentgenological study was made of 256 cases which had had thoracoplasty. Preoperative scoliosis was found in 30 of these, 11.7 per cent, and the remainder had perfectly straight spines. Postoperative scoliosis developed in 219 of the 256 patients, 85 per cent. There were no significant differences in the sexes, nor did the state of nutrition of the patient have any effect upon the development of scoliosis. In all cases the convexity of the curvature of the spine was toward the side of operation. A greater severity of scoliosis was noted as the lower ribs were removed. Fifty per cent of the patients developed scoliosis after a one-stage

thoracoplasty and 96.2 per cent after a three-stage thoracoplasty. The most important causative factor in the production of scoliosis following thoracoplasty seems to be the removal of the transverse processes of the vertebra. In not one case in which the transverse processes were not resected did scoliosis develop. It is believed that the cause of the scoliosis is not so much the resection of the transverse processes as it is the destruction of the muscles and ligaments which have their origins or insertions on the transverse processes and which act as restraining bands in keeping the spine straight. It is furthermore believed that removal of the transverse processes of the vertebra is not essential to the effective closure of pulmonary cavities. Therefore it is perhaps best that the transverse processes be left intact to insure against the development of postoperative scoliosis.—*The Role of the Transverse Process in Thoracogenic Scoliosis, H. L. Wenger & M. Herman, Quart. Bull. Sea View Hosp., October, 1941, 7: 45.*—(*A. A. E.*)

Extrapleural Pneumothorax.—The technique of extrapleural pneumothorax is described and the importance of postoperative care is pointed out. Frequent X-ray examination is advised. The most common and serious complication is bleeding into the extrapleural space. Extrapleural pneumothorax is indicated when intrapleural pneumothorax has failed. It produces less shock than thoracoplasty, is less deforming, especially in young people during the growing stage, and it can be stopped and the lung can reëxpand. In 3 patients with intrapleural pneumothorax with uncuttable adhesions an extrapleural pneumothorax was induced over the adhesions; the extrapleural space was connected with the intrapleural cavity. All these cases had a very stormy postoperative course. In 5 cases the extrapleural space was later filled with oil in order to maintain the collapse; 3 of these were later observed and were doing well. Extrapleural pneumothorax was attempted in 39 patients. In 5 patients extensive adhesions made the operation impossible. Five patients are still under treatment, 6 had later a thoracoplasty. Of the remaining 23 patients, 12 were discharged as much improved, 3 as improved, 8 obtained no improvement; 13 of these became sputum-negative. One patient died of secondary haemorrhage forty-eight hours after the operation; one patient died four days after the operation due to pressure of a pleural effusion on the heart. In 8 patients there was a subsequent infection of the extrapleural space; in 3 of these thoracoplasty was done later.—*Extrapleural Pneumothorax—Its Scope and Limitations, P. V. Benjamin, Indian M. Gaz., October, 1941, 76: 577.*—(*G. C. L.*)

Pleural Adhesions.—Before a pneumonolysis is performed, position, shape and anatomical structure of the adhesions should be examined. Transillumination of adhesions permits their anatomical investigation. The pleuroscopic models of Kalk and Graf allow transillumination of adhesions and simultaneous cauterization. The advantage of these instruments was proven in more than 200 operations.—*Transillumination and Simultaneous Cauterization of Pleural Adehsions, K. Eisenstaedt & A. U. Rindani, Indian M. Gaz., October, 1941, 76: 581.*—(*G. C. L.*)

Intracavitary Drainage.—Technique and dangers of the Monaldi procedure are discussed. It should not be done before it has been shown that there is complete pleural obliteration. A case is reported in whom intracavitary drainage was instituted. The size of the cavity diminished within a short time. The amount of sputum decreased, the number of tubercle bacilli in the drainage from the cavity diminished considerably.—*Drainage cavitaire suivant la méthode de Monaldi, L. Rousseau, Laval méd., March, 1942, 7: 152.*—(*G. C. L.*)

Intracavitary Drainage.—The author summarizes his experiences in 56 cases which have been treated with Monaldi intracavitary drainage. The theoretical considerations which make the procedure successful are

briefly reviewed. The direct effects of drainage are removal of the cavity contents and cleaning of cavity walls, shrinkage of the size of the cavity through maintaining a subatmospheric intracavitary pressure and reaeration of pericavitary atelectatic areas. The indication is a preferably isolated cavity in relatively normal lung tissue. There must be no free pleural space and, preferably the patient should be nontoxaemic and fever-free before the procedure is begun. Accurate localization with the aid of tomography and fluoroscopy is essential, but cavities can be drained with equal success no matter what their location. In the author's experience no mortality has accompanied the procedure although air embolism and haemorrhage are theoretically possible. Complications are few, the only fairly common one being infection of the soft tissue tract. Although a number of patients are still under treatment, many have been discharged cured. In certain cases the draining bronchus does not close spontaneously after institution of drainage and cauterization of the bronchial lumen has been attempted. Certain cases have been subjected to thoracoplasty for closure of residual cavities, and in all these cases it is fair to state that thoracoplasty without preceding drainage would have been impossible.—*Über die Behandlung der kavernösen Lungentuberkulose mit der Kavernensaugdrainage, A. Schuberth, Schweiz. med. Wchnschr., November 8, 1941, 71: 1412.*—(*H. M.*)

Open Cavity Drainage.—A successful result is reported in a case in which pneumonotomy and external drainage was performed for a cavity which had persisted after four stages of thoracoplasty.—*Ouverture opératoire d'une caverne tuberculeuse du poumon. Guérison, O. Monod & X. Gellé, Rev. de la tuberc., 1939-1940, 5: (no. 13), 1481.*—(*H. L. I.*)

Pneumoperitoneum. — By pneumoperitoneum the diaphragm is raised and its respiratory excursions are diminished. Thus the vertical movements of the lungs are reduced. Forty-nine patients, who were either too ill for collapse therapy or in whom collapse therapy was ineffective, received pneumoperitoneum. Eleven of these were treated less than one month. Cough, expectoration, digestive disturbances diminished. In 2 cases haemoptysis was controlled. In some cases considerable improvement was seen radiologically. The sputum turned negative for tubercle bacilli only in 3 cases. The initial fill should not be more than 200 cc. Refills of 600 to 800 cc. should be given twice a week, later once a week. If the diaphragm cannot rise due to adhesions pneumoperitoneum is not of benefit. Complications were: peritoneal shock in 3 cases, subcutaneous emphysema in a few cases, a large haematoma in 3 cases.—*Pneumo-Peritoneum in the Treatment of Advanced Pulmonary Tuberculosis, L. R. Dongrey, Indian M. Gaz., October, 1941, 76: 587.*—(*G. C. L.*)

Demonstration of Tubercle Bacilli.—A comparison was made of various methods for demonstrating tubercle bacilli by concentration methods. Acids, alkalis, animal ferments, vegetable ferments, organic solvents, chemical flocculation and surface tension depressors were compared with the sodium hydroxide method. The wide variation in results obtained through the use of various methods of digesting sputa and gastric specimens and precipitating the tubercle bacilli from the digests indicates that the newer methods of handling have little, if any, advantage over digestion with normal sodium hydroxide (2 per cent sodium hydroxide with gastric contents or less mucoid sputa) and long centrifugation. Comparable results in precipitating the organisms can be obtained through a fairly wide range of pH values (9 to 11) and surface tension reading (63 to 73). Dilution with distilled water or alcohol to lower specific gravity was of no value except in the case of very viscous specimens. In such cases dilution with distilled water before digestion aids in liquefaction, and it is not necessary to increase the concentration of the digester. The use of a large amount of specimen, thorough liquefaction and long

centrifugation, thus securing a great concentration of solids, are the essentials of a good concentration method.—*Factors Influencing the Demonstration of Tubercle Bacilli by Concentration Methods, L. Robinson & W. D. Stovall, J. Lab. & Clin. Med., October, 1941, 27: 84.*—(*F. G. P.*)

Gastric Lavage.—In the literature there are reported altogether 910 observations of gastric juice of tuberculous children a few months to fifteen years of age; 373 (40 per cent) were positive for tubercle bacilli. The gastric juice of 110 children with primary infection was examined at the *Hôpital Laval.* The children were a few months to twelve years old. Thirty-two were positive on direct smear, 23 were found positive by guinea-pig inoculation.—*Le lavage gastrique dans la primo-infection de l'enfant, M. Giroux, Laval méd., February, 1942, 7: 102.*—(*G. C. L.*)

Sputum Enrichment.—Bekker compared the efficiency of the antiformin and the S.E.S. methods of demonstrating tubercle bacilli in the sputum. The latter method is carried out as follows: to 5 cc. of sputum is added 3 cc. of a mixture of equal parts of 10 per cent sulfuric acid and 10 per cent iron sulfate ($FeSO_4 \cdot 7\ H_2O$). This dissolves the mucus. To the homogenized sputum is now added 3 cc. of 3 per cent hydrogen superoxide and the mixture is centrifuged. The sediment is washed with 2 per cent sodium lactate and again centrifuged. It can then be stained or used for culture and inoculation. This method, when applied on some 380 sputa and compared with the antiformin method on the same number of sputa, gave no essentially different results. Furthermore treatment of sputum with sulfuric acid as compared with the S.E.S. method gave approximately the same number of positive cultures.—*Der Tuberkelbazillennachweis in Sputum (Vergleichende Untersuchungen über das S.E.S. Verfahren und die Antiforminanreicherung), J. H. Bekker, Zentralbl. f. Bakt., Orig., January, 1941, 146: 347.*—(*M. B. L.*)

Trypsin Digestion of Sputum.—Since 1933 specimens such as sputum, stomach washings, pleural and abdominal fluids, urine that contained mucus and pus from abscesses have been digested with an aqueous solution of trypsin with satisfactory results. The trypsin solution is prepared as follows: a 0.5 per cent trypsin solution (Trypsin 1:250 Difco) in sterile water is mixed by shaking and 0.7 per cent N/1 sodium hydroxide solution is added which gives approximately pH 8.5. An equal quantity of the trypsin solution is added or more if the specimen is very thick, and mixed thoroughly with an applicator or glass rod. Incubate at 37°C. for thirty minutes, or until the mucus is thoroughly digested; stirring after ten to fifteen minutes incubation may hasten digestion. The specimen is then centrifuged at 3,000 r.p.m. for five minutes, or at 1,500 r.p.m. for ten minutes. A loopful of the sediment is smeared on a glass slide, fixed and stained by the Ziehl-Neelsen method. If the smear is thin, methylene blue is used as a counterstain; if it is thick, 1 per cent aqueous picric acid is used. The sediment is also satisfactory for examination by the fluorescence method. In a comparative study of this method and the flocculation method of Hanks *et al.*, of 100 positive specimens, 11 per cent more positives were found by the trypsin method. In 71.5 per cent of the smears made from the trypsin-digested portion of the specimens more acid-fast bacilli were found than in smears made from the flocculation concentrate, and in 30 per cent of these at least twice as many bacilli were found. In contrast to these results, only 28.4 per cent of the smears made from the flocculation concentrate showed more bacilli than those made from the trypsin-digested portion of the specimen, and of these, only 7 per cent showed twice as many or more acid-fast bacilli.—*Trypsin as a Digestant of Sputum and Other Body Fluids Preliminary to Examination for Acid-Fast Bacilli, E. Haynes, J. Lab. & Clin. Med., March, 1942, 27: 806.*—(*F. G. P.*)

Sputum Film Cultures of Tubercle Bacilli.—The author reports a microculture method that increased the rapidity of growth of tubercle bacilli. He incubated sulfuric acid-treated films of tuberculous sputum in the presence of haemolyzed human blood. After forty-eight hours, obvious signs of growth of the colonies were perceptible with the low power objective; after seventy-two hours, distinct growth could be seen. At the end of one week the cultures were well grown. The author has grown colonies of tubercle bacilli on slides, in Petri dishes and in screw-capped bottles and found that the method is successful by all of these means. Most luxuriant growth is obtained when the microculture is exposed to moist air. Typical colonies are long and stringy, later becoming twisted and coiled, but compact and bushy forms do occur. Considerable morphological differences are found in the stained bacilli in different cases and sometimes between different colonies in the same culture. In most week-old cultures the author found branching mycelial threads about 20 micra long. The author suggests that the method is of interest in providing a ready means of studying early growth; it may prove useful as a routine procedure.—*Sputum Film Cultures of Tubercle Bacilli: A Method for the Early Observation of Growth, D. M. Pryce, J. Path. & Bact., November, 1941, 327: 324.*—(*H. J. H.*)

Growth Promotion by Serum Albumen.—Crystalline horse serum albumen was shown to be strongly growth-promoting for tubercle bacilli grown in synthetic media. The globulins were without effect or inhibited growth. —*Growth Promotion of the Tubercle Bacillus by Serum Albumen, C. H. Boissevain, Proc. Soc. Exper. Biol. & Med., May, 1940, 44: 110.* —(*F. B. S.*)

Bacteriostatic Action of Wetting Agents. —Several neutral wetting agents were tested for bacteriostatic effect on the nonvirulent Novy strain of tubercle bacillus and their order of effectiveness was as follows: Zephiran, a mixture of high molecular alkyl-dimethyl-benzyl-ammonium chlorides; Nacconol NR, an alkyl aryl sulfonate; Aerosol OT-100, an ester of a sulfonated bi-carboxylic acid; and Aerosol OS, a sodium salt of an alkyl naphthalene sulfonic acid. Although complete bacteriostatic action of Zephiran against tubercle bacilli occurred in dilutions as high as 1:80-000, the bactericidal action was low. Its superior action over the other compounds was probably inherent in its molecular structure. —*Bacteriostatic Action of Various Wetting Agents upon Growth of Tubercle Bacilli in vitro, B. L. Freedlander, Proc. Soc. Exper. Biol. & Med., May, 1940, 44: 51.*—(*F. B. S.*)

Chlorophyll Pigment and Tuberculosis.—Chlorin-e-rhodin-g inhibited the growth of human and bovine tubercle bacilli *in vitro*, but had no effect on the course of experimental tuberculosis in rabbits. The pigment accumulated in large quantity in phagocytic cells in the spleen, bone marrow and in cells on the border of tubercles.—*Effect of Chlorin-e Rhodin-g on Experimental Tuberculosis, H. J. Henderson & E. R. Long, Proc. Soc. Exper. Biol. & Med., November, 1941, 48: 435.*—(*F. B. S.*)

Aetiology of Tuberculosis.—An attempt has been made to determine the mode of spread of tubercle bacilli from the infectious patient to other individuals. The tubercle bacillus does not propagate outside of the living body. Infection as a rule occurs through exposure to the bacillus by close contact with infected secretions. In the present study an effort was made to determine whether tuberculosis could be transmitted through the agency of books and clothing used by patients with sputum which contained tubercle bacilli. In the examination of books the patients were instructed to use the books carelessly and to cough and breathe upon the pages. The contaminated pages were then scraped with sterile razor blades and the scrapings suspended in a saline solution, portions of which were then injected into guinea pigs. None of the injected animals

developed tuberculosis. A similar method was used in obtaining tubercle bacilli from clothing, except that in addition to injection guinea pigs were also exposed to inhalation of the scrapings. Again no infection was found to take place. Therefore it has been impossible to demonstrate viable tubercle bacilli on books or clothing used or worn by patients with tuberculosis and positive sputum. It is suggested that books handled by tuberculous patients should be stored for several weeks in order to render completely sterile all bacilli that might have been deposited upon them.—*Aetiological Studies of Tuberculosis, I, M. A. Jacobs & S. A. Petroff, Quart. Bull. Sea View Hosp., October, 1941, 7:33.*—(*A. A. E.*)

Protein and Carbohydrate from Variants of Tubercle Bacilli.—A greater yield of organisms was obtained on synthetic medium from an Ra (rough avirulent) variant tubercle bacillus than from an Rv (rough virulent) variant from the single parent strain H37. Both variants had been stable for five years in appearance and in virulence for guinea pigs. A greater yield of PPD and carbohydrate was obtained from the tuberculin produced by Rv organisms. Both PPD's gave specific skin reactions in guinea pigs inoculated with either variant, but no differencel was noted between the two preparations. A difference between the two carbohydrates was found by means of the precipitin test in goat antisera, although definite cross precipitation was also noted.—*The Isolation of Purified Protein Derivatives and Carbohydrates from Tuberculins and Their Biological Properties, W. Steenken, Jr., J. Biol. Chem., October, 1941, 141: 91.*—(*F. B. S.*)

X-ray Studies on Tuberculin Proteins.—The X-ray diffraction patterns of tuberculin proteins, after the effects of buffer salts, polysaccharides, and nucleic acid impurities are accounted for, show spacings at 4.43 to 4.60 Å and 9.64 to 10.6 Å. These spacings are within the range observed for other proteins under similar conditions. In three samples diameters of approximately 20 Å were computed for particle size by the method of Sherrer. These values are in good agreement with molecular diameters calculated from the densities and the molecular weights of the tuberculin proteins determined by ultra-centrifugation.—*X-ray Studies on Tuberculin Proteins, Mona Spiegel-Adolf, F. B. Seibert & G. C. Henny, J. Biol. Chem, February, 1941, 137: 503.*—(*F. B. S.*)

Tuberculin Polysaccharide and Nucleic Acid.—A relatively simple scheme was given for making a rough separation of the protein, nucleic acid, and polysaccharide fractions of tuberculin in large quantities. Further separation of these fractions by means of the Tiselius electrophoresis apparatus yielded two types of polysaccharide. One did not migrate in the electrical field, was colorless and contained only about 0.2 per cent nitrogen. The other, present in much larger quantity, had a low mobility, and the nitrogenous impurity could not be removed to less than 0.85 per cent nitrogen, even by prolonged electrophoresis. Nucleic acid was also isolated in small amount and its purity was demonstrated by chemical analysis as well as by electrophoretic analyses.—*Isolation of the Polysaccharides and Nucleic Acid of Tuberculin by Electrophoresis, Florence B. Seibert & D. W. Watson, J. Biol. Chem., July, 1941, 140: 55.*—(*F. B. S.*)

Nucleic Acid and Polysaccharide of Tuberculin.—Electrophoretic studies, using the Tiselius technique, demonstrated that nucleic acid could be removed from the tuberculin protein on the alkaline side of pH 5.0, whereas on the acid side it remained attached to the protein during any precipitation. Therefore, precipitation of tuberculin protein at pH 7.0 by half saturation with ammonium sulfate removed the nucleic acid with no loss in potency. Tuberculin polysaccharide was immobile at all pH values and was, therefore, also removed during the precipitation.—*Removal of the Impurities, Nucleic Acid and Polysaccharide, from Tuberculin Protein, Flor-*

ence B. Seibert, J. Biol. Chem., April, 1940, 133: 593.—(F. B. S.)

Polysaccharide of Tubercle Bacilli.—The polysaccharide fractions of the phosphatides prepared from bacterial residues from tuberculin manufacture were not identical with the polysaccharide in the phosphatide prepared from living tubercle bacilli of strain H37. Two polysaccharide fractions isolated from two such phosphatide preparations gave different cleavage products. Both gave on phosphorylation free inosite and a glycoside. The glycoside, in one case, gave on hydrolysis mannose and some other reducing sugar, and, in the other case inosite also was obtained. The reducing sugars other than mannose gave typical glucosazones. Glycoside manninositose was not found in either case. The organic phosphoric acids separated from the polysaccharides were of two kinds: (*a*) an acid corresponding approximately in composition to inosite monophosphoric acid, and (*b*) an acid corresponding to glycerophosphoric acid.—*The Chemistry of the Lipids of Tubercle Bacilli, LXI. The Polysaccharides of the Phosphatide Obtained from Cell Residues in the Preparation of Tuberculin, R. J. Anderson, R. L. Peck & M. M. Creighton, J. Biol. Chem., October, 1940, 136: 211.* — *(F. B. S.)*

Polysaccharides of Avian Tubercle Bacillus.—The total amount of polysaccharide isolated from an avian strain of the tubercle bacillus, was less than from human and bovine strains, but the proportion of serologically active material was intermediate between them. The specific polysaccharides showed the same immunological specificities as in the human and bovine types and the serological activity was highest in the fractions containing pentose. No soluble serologically inactive, phosphorylated carbohydrate corresponding to that found in the bovine strain was encountered.—*Specific and Non-Specific Cell Polysaccharides of an Avian Strain of Tubercle Bacillus, S. A. Karjala & M. Heidelberger, J. Biol. Chem., January, 1941, 137: 189.*—*(F. B. S.)*

Phleimycolic Acid in Tubercle Bacilli.—The principal ether-soluble component of the wax of the timothy bacillus is a dibasic acid corresponding approximately to the formula $C_{70}H_{138}O_6$. The properties of this acid are similar to those of the mycolic acids and hence it has been designated by the name phleimycolic acid.—*The Chemistry of the Lipids of Tubercle Bacilli, LXIV. Concerning Phleimycolic Acid, R. L. Peck & R. J. Anderson, J. Biol. Chem., July, 1941, 140: 89.*—*(F. B. S.)*

Fatty Acids in Tubercle Bacilli.—The fatty acids were obtained from phosphatide prepared from bacterial residues from the manufacture of tuberculin. The solid saturated acids consisted mainly of palmitic acid and traces of stearic and mycolic acids. The liquid unsaturated acid was mainly oleic acid, since after catalytic reduction chiefly stearic acid was found. The liquid saturated fatty acids consisted mainly of tuberculostearic acid, $C_{19}H_{38}O_2$. A small amount of higher branched chain dextrorotatory acids was present, which were not definitely identified. No pure phthioic acid was found.—*The Chemistry of the Lipids of Tubercle Bacilli, LXIII. The Fatty Acids in the Phosphatide Prepared from Cell Residues from Tuberculin, R. L. Peck & R. J. Anderson, J. Biol. Chem., March, 1941, 138: 135.*—*(F. B. S.)*

Lipids of Avian Tubercle Bacilli.—Avian tubercle bacilli after thorough extraction with neutral solvents yielded 10.8 per cent of firmly bound lipids on treatment with dilute hydrochloric acid and extraction with ether and chloroform. The firmly bound lipids were separated into filtrable and unfiltrable fractions by forcing a chloroform solution of the mixture through a Chamberland filter. The unfiltrable lipid gave on saponification 64 per cent of ether-soluble constituents and 31 per cent of a water-soluble polysaccharide. (*a*) The ether-soluble components consisted of 76.2 per cent hydroxy acids of high molecular weight and unknown constitution, 5.6 per

cent of lower fatty acids, and 15.5 per cent of neutral material. (*b*) The neutral material consisted mainly of d-eicosanol-2, $CH_3(CH_2)_{17}CHOHCH_3$. (*c*) The polysaccharide gave on hydrolysis 50.1 per cent of reducing sugars consisting of mannose, d-arabinose, and galactose, together with traces of glucosamine and inosite. The solid portion of the filtrable lipid gave on saponification 80.9 per cent of ether-soluble components and 15.0 per cent of polysaccharide. (*a*) The ether-soluble components consisted of 69.0 per cent of hydroxy acids, 3.7 per cent of lower fatty acids, and 8.2 per cent of neutral material. (*b*) The neutral material consisted mainly of d-eicosanol-2. (*c*) The hydroxy acid, named avian γ-mycolic acid, was split on heating to 270-280° under reduced pressure, and gave a crystalline acid which distilled off, leaving an unsaturated non-volatile residue. (*d*) The acid liberated on pyrolysis corresponded in composition to a tetracosanoic acid, $C_{24}H_{48}O_2$, but it differed in crystal form from the ordinary straight chain fatty acids. —*The Chemistry of the Lipids of Tubercle Bacilli, LX. Concerning the Firmly Bound Lipids of the Avian Tubercle Bacillus, R. J. Anderson, M. M. Creighton & R. L. Peck, J. Biol. Chem., May, 1940, 133: 675.*—(*F. B. S.*)

Riboflavin in Tubercle Bacillus.—Tubercle bacilli cultivated on Long synthetic medium were extracted with warm 25 per cent alcohol. The extract showed yellowish-green fluorescence in ultraviolet rays and the amount of flavin was determined quantitatively after conversion to lumiflavin and analysis by the Pulfrich spectrophotometer. This flavin extract was then fed to rats on a riboflavin-deficient diet and the growth curves indicated that it possessed the same biological activity as crystalline riboflavin.—*Occurrence of Riboflavin in Tubercle Bacillus, H. R. Street & R. E. Reeves, Proc. Soc. Exper. Biol. & Med., June, 1940, 44: 641.*—(*F. B. S.*)

Biological Activities of Purified Tuberculins.—Quantitative precipitation of various purified tuberculin preparations, with trichloracetic acid, utilizing the Hopkins tube method, was useful for the estimation of their biological activity.—*Estimation of Biological Activities of Purified Tuberculin by the Hopkins Tube, S. C. Wong & G. Ouyang, Proc. Soc. Exper. Biol. & Med., April, 1941, 46: 615.*—(*F. B. S.*)

Stability of Dilute Purified Tuberculins.—A preparation of purified tuberculin was diluted with neutral phosphate buffer, containing 0.5 per cent phenol, so that 0.1 cc. contained 0.000,02 mg. After four months at 20° or six months at 8°C. no deterioration in potency occurred when compared with PPD, although the latter elicited stronger reactions in a larger number of positive reactors.—*Studies on Stability of Dilute Purified Tuberculins, S. C. Wong & G. Ouyang, Proc. Soc. Exper. Biol. & Med., October, 1940, 45: 83.*—(*F. B. S.*)

Purified Tuberculin from Bacterial Bodies.—Tubercle bacilli, from which the liquid medium had been decanted, were allowed to autolyze over sterile 0.05 normal sodium hydroxide. On the fourteenth day few intact cells were found, whereas in control flasks, where distilled water was used, comparatively little cellular disintegration occurred. Half of the autolysate was adjusted to pH 6.0 to 6.5, before heating at 100°C. for three hours, and half was not adjusted. Equal amounts of purified tuberculin could be precipitated from the two extracts, but that obtained from the unadjusted portion was not able to produce the skin reaction and was non-antigenic, whereas the other had about the same potency as PPD. Approximately three times as much purified tuberculin was obtained from these extracts as from the original culture liquid decanted away.—*Studies on Purified Tuberculin Prepared from Bacterial Bodies, S. C. Wong & G. Ouyang, Proc. Soc. Exper. Biol. & Med., December, 1940, 45: 845.*—(*F. B. S.*)

Tuberculins and Skin Reaction.—The present investigation concerns the physical-

chemical properties and the antigenicity of a number of chemically purified tuberculins prepared from avian, bovine and human tubercle bacilli; and the relation of these characteristics to the intracutaneous activity of a tuberculin. The different preparations of tuberculin were made from the same strains of either human, bovine or avian tubercle bacilli, but the methods differed somewhat. The tuberculins were prepared by Dr. Seibert in accordance with her methods of chemically purifying tuberculin proteins. The more antigenic tuberculins, namely, tuberculins 69-2 (avian), 49608 (human), and 61 (bovine), were steamed for not more than four hours, whereas tuberculin 67-2 (human) had been steamed three hours and then evaporated on a steam bath and in the presence of glycerine to one-fifth of the original volume of the culture filtrate. Tuberculin 69 was separated from 69-2 by precipitation at pH 4.3 and 67 was similarly separated from 67-2. The various phenomena described were observed only in the human being. Two different populations were represented; an urban group of university students, the majority of whom live in towns or have worked in towns, and the agricultural short-course students all of whom were farmers. The students tested were men from sixteen to twenty-five years of age, most of them being between eighteen and twenty-one. Two doses were used, 0.000,02 mg. and 0.005 mg. Reactions after forty-eight hours were obtained in 28.3 per cent of 1,344 urban students and 20.2 per cent of 692 rural students with human 67-2; 46.2 per cent of 173 rural students reacted to human 67; 54.5 per cent of 147 rural students reacted to human 49608. Twenty-five and six-tenths per cent of 394 urban students reacted to bovine 1; 66.4 per cent of 140 urban students and 61.4 per cent of 394 rural students reacted to bovine 61. Forty-six and one-tenth per cent of 739 urban students and 54.7 per cent of 287 rural students reacted to avian 1; 86.1 per cent of 65 urban students and 76.9 per cent of 182 rural students reacted to avian 69.2. Preliminary observations suggested that reactions to the more active tuberculins appeared earlier. A group of rural students were therefore tested with three human tuberculins of differing activities and readings were taken at six, twenty-four and forty-eight hours. One hundred per cent of 148 students reacted with human 49608 when readings were made at six hours, 77.9 per cent at twenty-four hours and 54.4 per cent at forty-eight hours. Two and nine-tenths per cent of 173 students reacted with human 67 when readings were made at six hours, 46.2 per cent at twenty-four hours and 46.2 per cent at forty-eight hours. One and two-tenths per cent of 173 students reacted with human 67-2 at six hours, 22.6 per cent at twenty-four hours, and 23.1 per cent at forty-eight hours. The same rural students were tested with the three tuberculins. The possibility of reactions to polysaccharides in tuberculin were also studied. The early six hour reactions are not elicited by tuberculin-polysaccharides. The protein present in tuberculin-polysaccharides and in tuberculo-polysaccharides is responsible for any skin-activity they may have. Some individuals give six-hour reactions to non-antigenic tuberculin-proteins. The more active tuberculin avian 1 and bovine 61 sensitized some individuals while the less active tuberculin 67-2 did not; about 30 per cent of the students retested gave small reactions to strong doses of preparation 1 or 61 six months after they had failed to react to the same tuberculins, while only 3 per cent gave such reactions upon retest with 67-2. All the students who reacted upon retest to a tuberculin of low activity were positive at the time of the first test to a tuberculin of greater activity such as avian 1. This must mean that the changing of a tuberculin-reaction from negative to positive within six months is not proof of infection with tubercle bacilli in the interim. No one of the students becoming positive upon retest to either tuberculins 1, 61 or 67-2 had developed lung-lesions of tuberculosis detectable by fluoroscopic examination at the time of retest nor of those followed by repeated fluoroscopic examinations. This indicated that the activity of a

tuberculin might be correlated with its antigenicity, and so the tuberculins were tested for their ability to induce precipitin-formation in rabbits. The tuberculins tested all induced Arthus reactions in rabbits, the most active tuberculins 69, 69-2, 61 and 49608, calling forth the largest resctions, 67 somewhat less of a reaction and 67-2 the least reaction. The antigenicity of the tuberculin-protein is destroyed when the molecule is degraded by heat to a weight of about 6000, but for molecules of over 12,000 and up to 36,000 the size bears no relation to antigenicity. From the data on the physical constants of these tuberculins, what apparently happens is that the native tuberculin-protein which is globular and about 17,000 to 32,000 in molecular weight, becomes unfolded and thus elongated by the steaming with no loss in weight and only slight reduction in antigenicity. The tuberculin reaction is quantitatively specific from the standpoint that all individuals with active tuberculosis give delayed reactions (lasting forty-eight hours) to very small doses of non-antigenic tuberculins. A typical active case of tuberculosis in a student was not found who had not reacted to tuberculin 67-2. Can we be sure, however, that even all those students who react to a non-antigenic tuberculin have been infected with mammalian tubercle bacilli when 70 per cent of them fail to show either healed or active lesions of tuberculosis on X-ray examination? The regulation of the time of reading reactions and of the antigenicity of the tuberculin used made it possible to secure reactions in 100 per cent of a population with a low incidence of tuberculosis. These students may have been sensitized, of course, by human or bovine tubercle bacilli. But only about 40 per cent of the tuberculin-reacting cattle in Wisconsin now being slaughtered show evidence, upon autopsy, of infection with mammalian tubercle bacilli. Some of the no-lesion, tuberculin-reacting cattle, as well as some of the cattle which show tuberculous lesions, have been shown to be infected with avian tubercle bacilli only and not with mammalian tubercle bacilli; and tuberculin-reacting cattle with so-called "skin" lesions only are not infected with tubercle bacilli but probably with some other member of the acid-fast group of bacteria. It seems probable that these students, as well as the cattle, have been sensitized to tuberculin by acid-fast bacteria other than mammalian tubercle bacilli; or by some other protein similar antigenically to the tuberculin-protein; or that a tuberculin may because of its own toxicity cause an inflammatory reaction in an unsensitized individual.—*The Relationship of the Antigenicity, Physical-Chemical Properties, and Polysaccharide-Content of Tuberculins to Their Intracutaneous Activity, J. R. McCarter & D. W. Watson, J. Immunol., January, 1942, 43: 85.*—(*F. G. P.*)

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